

REMARKS

Claims 1-20 are pending in the application. Claim 1 has been amended to further clarify the present invention.

Restriction Requirement

In the Office Action of February 18, 2005, the Examiner has divided the claims into four (4) groups: Group I, claims 1-2, 6, 14 and 18, drawn to a detoxified protein; Group II, claims 3-5, 7-9, 15-17 and 19-20, drawn to a DNA, vector and host cell; Group III, claims 10-11, drawn to a method of preparing a detoxified protein; and Group IV, claims 12-13, drawn to a vaccine and mucosal adjuvant.

Applicants traverse this requirement. Reconsideration and withdrawal thereof are earnestly requested.

First of all, the present application is a national phase application of a PCT application filed under 35 U.S.C. 371. Accordingly, unity of invention rules apply.

The Examiner indicates that the inventions listed as Groups I-IV do not relate to a single general inventive concept based on the following reasons: "The special technical feature of Group I is a detoxified protein. The special technical feature lacks novelty ... Domenighini et al. teach detoxified proteins of cholera toxins or heat labile toxins produce by *E. coli* which have a substitution at amino acid 63... Group I is the main invention in this application and it lacks novelty, therefore, the other claims are not so linked by a special technical feature with the meaning of PCT Rule 13.2 so as to form a single inventive concept." Applicants traverse this assertion of lack of unity of invention by the Examiner. Reconsideration and withdrawal thereof are earnestly requested.

Domenighini et al. (EP 0 620 850 B1, March 3, 1999)

Domenighini et al. discloses the amino acid sequence of subunit A of a cholera toxin (CT-A) or the amino acid sequence of subunit A of an *Escherichia coli* heat labile toxin (LT-A)

wherein serine at position 63 is replaced with lysine. However, Domenighini et al. fails to disclose substitution of the same position 63 with any other amino acid except for lysine.

The PCT Rule 13.2 defines the “special technical features” as those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. The detoxified protein of the present invention contributes over Domenighini et al. since Domenighini et al. does not teach a detoxified protein having an amino acid sequence of heat labile enterotoxin of *E. coli* in which serine residue at position 63 is substituted with tyrosine, and thus is novel over Domenighini et al., which discloses substitution of position 63 only with lysine. Therefore, Applicants assert that the inventions listed as Groups I-IV are linked by a special technical feature and form a single inventive concept. Accordingly, all of the claims should be examined together on the merits. At the least, the grouping separating out the method of preparing the product claims should be held in abeyance until allowable subject matter is found in the product claims, and then rejoined and considered at that time, as provided for under *In re Ochiai* and *In re Brouwer*.

Although Applicants disagree with the Examiner, in order to be responsive to the outstanding Lack of Unity Requirement, Applicants provisionally elect to prosecute Group I claims 1-2, 6, 14, and 18 drawn to a detoxified protein. Applicants specifically preserve the right to prosecute the non-elected claims.


Preliminary Amendment

Claim 1 of the present application has been currently amended to point out and distinctly claim the subject matter which applicants regard as the invention. Support for the amendment to claim 1 can be found at *inter alia* pages 10-11 of the specification. No new matter has been inserted into the application. Accordingly, early examination on the merits is respectfully requested.

The Commissioner is authorized to charge Deposit Account 502486 for any fees due to secure entry of this amendment to the extent necessary.

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Respectfully submitted,



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